

## Multiple intravenous injections of allogeneic equine mesenchymal stem cells do not induce a systemic inflammatory response but do alter lymphocyte subsets in healthy horses.

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### Public Summary:

**INTRODUCTION:** Intravenous (IV) injection of mesenchymal stem cells (MSCs) is used to treat systemic human diseases and disorders but is not routinely used in equine therapy. In horses, MSCs are isolated primarily from adipose tissue (AT) or bone marrow (BM) and used for treatment of orthopedic injuries through one or more local injections. The objective of this study was to determine the safety and lymphocyte response to multiple allogeneic IV injections of either AT-derived MSCs (AT-MSCs) or BM-derived MSCs (BM-MSCs) to healthy horses. **METHODS:** We injected three doses of  $25 \times 10^6$  allogeneic MSCs from either AT or BM (a total of  $75 \times 10^6$  MSCs per horse) into five and five, respectively, healthy horses. Horses were followed up for 35 days after the first MSC infusion. We evaluated host inflammatory and immune response, including total leukocyte numbers, serum cytokine concentration, and splenic lymphocyte subsets. **RESULTS:** Repeated injection of allogeneic AT-MSCs or BM-MSCs did not elicit any clinical adverse effects. Repeated BM-MSC injection resulted in increased blood CD8(+) T-cell numbers. Multiple BM-MSC injections also increased splenic regulatory T cell numbers compared with AT-MSC-injected horses but not controls. **CONCLUSIONS:** These data demonstrate that multiple IV injections of allogeneic MSCs are well tolerated by healthy horses. No clinical signs or clinico-pathologic measurements of organ toxicity or systemic inflammatory response were recorded. Increased numbers of circulating CD8(+) T cells after multiple IV injections of allogeneic BM-MSCs may indicate a mild allo-antigen-directed cytotoxic response. Safety and efficacy of allogeneic MSC IV infusions in sick horses remain to be determined.

### Scientific Abstract:

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